

REMARKS UNDER 37 CFR § 1.111

Formal Matters

Claims 1-5, 8-12, 17-23, 27-33, 35, 42, 45 and 47 are pending after entry of the amendments set forth herein.

Claims 1-5, 8-14, 17-23, 26-33, 35, 37, 39, 42 and 45-47 were examined. Claims 1-5, 9-14, 20, 22, 23, 26-33, 35, 37, 39 and 45-47 were rejected. Claims 8, 17-19, 21 and 42 were allowed.

Claims 13-14, 37, 39 and 46 have been cancelled.

Support for the amendments to claims directed to a targeting construct and methods of producing the targeting construct can be found throughout the specification at, for example, pages 55-59, specifically, Examples 1-4. Additionally, support for amendments to claims directed to murine embryonic stem cells, transgenic mice exhibiting a homozygous disruption in cGMP phosphodiesterase alpha subunit gene and methods of producing said transgenic mice and cells isolated from said mice may be found throughout the specification, at, for example, page 2, lines 3-18, page 7, lines 14-17 and page 21, lines 18-19. Also, support for claims directed to methods of identifying agents may be found throughout the specification at, for example, page 25, lines 18-29 and page 39, lines 16-35. No new matter is added by these amendments. As such, entry of the above amendments is respectfully requested.

The amendments to the claims are made without prejudice to the pending or now cancelled claims or to any subject matter pursued in related applications. Moreover, the amendments are made solely to expedite prosecution of the application and are not intended to limit the scope of the invention. Applicants reserve the right to prosecute any cancelled subject matter at a later time or in a later filed divisional, continuation or continuation-in-part application.

Applicants respectfully request reconsideration of the application in view of the amendments and remarks made herein.

Rejection under 35 U.S.C. § 112, 1st Paragraph.

Claims 1-5, 10, 12-14, 27-33 and 45-47 stand rejected under 35 U.S.C. § 112, 1st paragraph, as lacking enablement. Specifically, it is asserted in the Office Action that claims 1-5 and 10 lack enablement because the claims "encompass rat as well as mouse targeting constructs

and are therefore still directed to subject matter that is not enabled by the disclosure.”

Accordingly, Applicants have amended the claims to be directed to “mouse targeting constructs.”

It is also asserted in the Office Action that claims 12-14, 27-33 and 45-47 “fail to properly limit the knockout mouse to a mouse that exhibits a phenotype that the skilled artisan would know how to use.” Applicants submit that claims 12, 27, 32 and 33 have been amended to refer to the mouse of claim 8. Claims 45 and 47 have been amended to refer to the mouse of claim 42. Applicants point out that the mouse of claims 8 and 42 exhibit phenotypes that a skilled artisan would know how to use. Claims 13-14 and 46 have been canceled.

Claims 12, 27-33 and 45-47 stand rejected under 35 U.S.C. § 112, 1st paragraph, as lacking adequate written description. Specifically, it is asserted in the Office Action that the “rejected claims fail to limit the knockout mouse to a mouse expressing a phenotype that was described in the disclosure.” As amended, claims 12, 27-33 and 45-47 refer to the mouse of claim 8 or claim 42. As such, each of the above-mentioned claims refers to a mouse with a particular phenotype that was described in the disclosure.

Claims 10, 23 and 26 have been rejected under 35 U.S.C. § 112, 1st paragraph, as lacking enablement. Specifically, the Office Action asserts that the above-mentioned claims lack enablement with respect to how to make a knockout animal “using any cell other than a mouse embryonic stem cell.” Accordingly, Applicants have amended claims 10 and 23 to be directed to embryonic stem cells. Claim 26 has been canceled.

Claims 11-14, 32, 37, 39 and 46 have been rejected under 35 U.S.C. § 112, 1st paragraph, as lacking adequate written description. Specifically, the Office Action asserts “the skilled artisan would not predict that it would be possible to assess modulation or function of cGMP phosphodiesterase . . . because a homozygous disruption in [the gene] would not express a measurable gene product.” Applicants have amended claims 11-23 and 32 to be directed to methods for identifying agents that ameliorate a phenotype associated with a homozygous disruption in a cGMP phosphodiesterase gene. Claims 13-14, 37, 39 and 46 have been canceled.

The Applicants submit that the rejections are overcome by the amendments. Applicants also submit that the amended claims are fully enabled by the teachings of the specification. Therefore, the Applicants submit that the rejection of above-cited claims under 35 U.S.C. § 112, first paragraph, is overcome in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw this rejection.

Rejection under 35 U.S.C. § 112, 2nd Paragraph.

Claims 9, 20, 22, 26, 33 and 45-47 have been rejected as being “indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.” Specifically, the Office Action suggests that replacing the term “derived” in claim 9 with the term “obtained” will obviate the rejection. The Applicants have adopted this suggestion. The Applicants submit that the rejection of claim 9 is overcome by this amendment and this rejection may be withdrawn.

It is also asserted in the Office Action that claim 20 is indefinite in that it “fails to limit claim 18 from which it depends.” The Office Action suggests that “by amending claim 20 such that it depends from claim 8 or 17” the rejection could be traversed. The Applicants have adopted this suggestion. As such, claim 20 depends from claim 8 and the Applicants submit that the rejection of claim 20 is overcome by the amendment and this rejection may be withdrawn.

It is also asserted in the Office Action that claim 22 is indefinite in being directed to a variety of eye abnormalities while claim 17, from which claim 22 depends, is limited to a retinal abnormality. The Office Action suggests that by amending claim 22 such that it depends from claim 8 or 17 the rejection could be traversed. The Applicants have adopted this suggestion. As such, claim 22 depends from claim 8 and the Applicants submit that the rejection of claim 22 is overcome by the amendment and this rejection may be withdrawn.

With respect to claims 27, 28-31 as they depend from claims 27, 33 and 45-47, the Office Action asserts that “each of the claims is indefinite in being directed to a method of measuring an alteration in a phenotype in a transgenic mouse, wherein the transgenic mouse is not limited to a mouse having the measured phenotype.” The Applicants have amended the above-mentioned claims to refer to the transgenic mouse of claim 8 or claim 42. Applicants point out that the transgenic mouse of claims 8 and 42 have a measurable phenotype. As such, Applicants submit that the rejection of the above-mentioned claims is overcome in view of these amendments. The Examiner is thus respectfully requested to withdraw this rejection.

Rejection under 35 U.S.C. § 103(a).

Claim 35 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Baehr et. al., FEBS letters vol. 278, no. 1 pp. 1070114 (1991), Lem et. al., Proc. Natl. Acad. Sci., USA,

vol. 89, no. 10 pp 4422-4427 (1992) and further in view of Tanabe et. al., IOVS vol. 39, no. 4 pp S1118 (1998). The Office Action asserts that the above-cited art describes "mice having homozygous disruptions of cGMP phosphodiesterase beta and gamma subunits and expressing abnormalities." Accordingly, Applicants have amended claim 35 to recite a "cGMP phosphodiesterase **alpha subunit** gene."

In view of the amendment to claim 35, Applicants submit that the obviousness rejection is overcome. Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103.

Claim Objections.

Claims 27 and 28-31, as they depend from claim 27 have been objected to because of a typographical informality: two semicolons following the word "gene." Applicants have corrected this typographical informality by deleting the duplicate semicolon. Applicants respectfully request withdrawal of this objection.

Conclusion

In view of the above amendments and remarks, the application is in good and proper form for allowance and the Examiner is respectfully requested to withdraw the rejections and pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (650) 569-5100.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-1271, order number R-849.

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DELTAGEN, INC.
700 Bay Road
Redwood City, CA 94063
Telephone: (650) 569-5100

Respectfully submitted,
DELTAGEN, INC.

By: Nicole A. Verona
Nicole A. Verona
Registration No. 47,153